AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (original) A method for detecting a predisposition to liver disease in an individual, the method comprising:

analyzing an individual for quantitative or qualitative change in phenotype or genotype of keratin K8 or K18.

2. (original) The method of Claim 1, wherein said liver disease is a noncryptogenic liver disease.

3. (original) The method of Claim 2, wherein said human keratin is one or more of K8 G52X; K8 Y53X; K8 G61X; K8 R340X; K8 G433X; K8 R453X; K18 T102X; K18 H127X; K18 I149X; K18 R260X; K18 E275X; K18 Q284X; K18 T294X; K18 T296X; and K18 G339X, where X is any amino acid other than the naturally occurring amino acid or a deleted amino acid.

4. (original) The method of Claim 2, wherein said human keratin is one or more of K8 G52V; K8 Y53H; K8 G61C; K8 R340H; K8 G433S; K8 R453C; and K8 1-465(I)RDT(468).

5. (original) The method of Claim 2, wherein said human keratin is one or more of K18 Δ64-71; K18 T102A; K18 H127L; K18 I149V; K18 R260Q; K18 E275G; K18 Q284R; K18 T294M; K18 T296I; K18 G339R.

6. (currently amended) The method of ~~any one of Claim 3-5~~ Claim 3, wherein said analyzing the genomic or mRNA sequences comprises the steps of:

amplifying a region of the K8 or K18 coding or noncoding sequences from isolated genomic DNA or mRNA to provide an amplified fragment;

detecting the presence of a mutated sequence in said amplified fragment.

7. (original) The method of Claim 6, wherein said detecting step comprises hybridization with a probe specific for said mutated sequence or digestion with specific restriction enzymes.

8. (currently amended) The method of ~~any one of Claim 3-5~~ Claim 3, wherein said detecting step comprising contacting a cell, tissue or potentially a serum sample with an antibody specific for one or more of said polymorphisms.

9. (original) A method of screening for biologically active agents that affect susceptibility to liver disease, the method comprising:

combining a candidate biologically active agent with any one of:

(a) a K8/K18 polypeptide comprising one or more of K8 G52X; K8 Y53X; K8 G61X; K8 R340X; K8 G433X; K8 R453X; K18 T102X; K18 H127X; K18 I149X; K18 R260X; K18 E275X; K18 Q284X; K18 T294X; K18 T296X; and K18 G339X, where X is any amino acid other than the naturally occurring amino acid or a deleted amino acid; the polypeptides may also comprise deletions in K8 and/or K18;

(b) a cell comprising a nucleic acid encoding a K8/K18 polypeptide comprising one or more of K8 G52X; K8 Y53X; K8 G61X; K8 R340X; K8 G433X; K8 R453X; K18 T102X; K18 H127X; K18 I149X; K18 R260X; K18 E275X; K18 Q284X; K18 T294X; K18 T296X; and K18 G339X, where X is any amino acid other than the naturally occurring amino acid or a deleted amino acid; or a cell that expresses a deletion of K8 and/or K18; or a cell expressing another K8 or K18 mutant that alters K8/K18 filament organization such as the K18 R89C which causes keratin filament collapse; or

(c) a non-human transgenic animal model for liver disease comprising an exogenous and stably transmitted gene encoding a K8/K18 polypeptide comprising one or more of K8 G52X; K8 Y53X; K8 G61X; K8 R340X; K8 G433X; K8 R453X; K18 T102X; K18 H127X; K18 I149X; K18 R260X; K18 E275X; K18 Q284X; K18 T294X; K18 T296X; and K18 G339X, where X is any amino acid other than the naturally occurring amino acid or a deleted amino acid; or a transgenic animal model expressing a deletion of K8 and/or K18; or a transgenic animal model expressing another K8 or K18 mutant that alters K8/K18 filament organization such as the K18 R89C which causes keratin filament collapse and

determining the effect of said agent susceptibility to liver disease.

10. (original) A polypeptide encompassing a keratin mutation selected from the group consisting of K8 G52X; K8 Y53X; K8 G61X; K8 R340X; K8 G433X; K8 R453X; K18 T102X; K18 H127X; K18 I149X; K18 R260X; K18 E275X; K18 Q284X; K18 T294X; K18 T296X; and K18 G339X, where X is any amino acid other than the naturally occurring amino acid or a deleted amino acid.

11. (original) A polypeptide according to Claim 10, wherein said mutation is selected from the group consisting of K8 G52V; K8 Y53H; K8 G61C; K8 R340H; K8 G433S; K8 R453C; and K8 1-465(I)RDT(468).

12. (original) A polypeptide according to Claim 10, wherein said mutation is selected from the group consisting of K18 Δ64-71; K18 T102A; K18 H127L; K18 I149V; K18 R260Q; K18 E275G; K18 Q284R; K18 T294M; K18 T296I; K18 G339R.

13. (currently amended) An antibody specific for a polypeptide as set forth in ~~any one of Claims 10-12~~ Claim 10.

14. (currently amended) A polynucleotide encoding a polypeptide as set forth in ~~any one of Claims 10-12~~ Claim 10.